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In Silico Models for Drug Discovery

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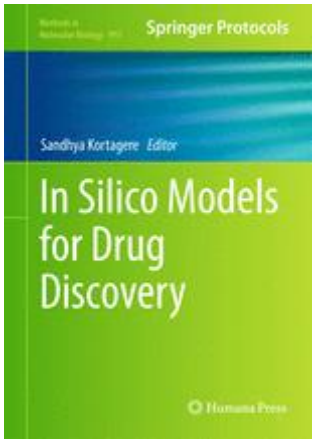
- Segun Fatumo
- , Marion Adebiyi
- , Ezekiel Adebiyi

Abstract

Resistance to drugs that treat infectious disease is a major problem worldwide. The rapid emergence of drug resistance is not well understood. We present two in silico models for the discovery of drug resistance mechanisms and for combating the evolution of resistance, respectively. In the first model, we computationally investigated subgraphs of a biological interaction network that show substantial adaptations when cells transcriptionally respond to a changing environment or treatment. As a case study, we investigated the response of the malaria parasite *Plasmodium falciparum* to chloroquine and tetracycline treatments. The second model involves a machine learning technique that combines clustering, common distance similarity measurements, and hierarchical clustering to propose new combinations of drug targets.

Key words

In silico Drug Resistance Model Mechanism

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Key words In silico, Drug, Resistance, Model, Mechanism

1 Introduction

Controlling infectious diseases is becoming more difficult as a result of the emergence of resistance to available drugs on the market. Drug resistance has emerged in the most dangerous diseases affecting humans, including malaria, tuberculosis, and HIV infection. These diseases have increased the disease burden particularly in developing countries, especially in Africa.

In this report, we present two in silico models, one for the discovery of drug resistance mechanisms and another for combating the evolution of drug resistance. Although we have adapted and developed these models for malaria research, they can be employed in the study of other infectious diseases. The first model has not been previously published. A model similar to our second model has been developed for the treatment of gastrointestinal stromal tumor (GIST) (1). With tumors as heterogeneous as GIST, up to five different types of secondary mutations can occur in the same patient. The aim is not only to wait for mutations to emerge before selecting the right compound but also to predict and group mutations according to likelihood, enabling clinicians to prescribe an appropriate drug as soon as a patient displays a particular mutation.

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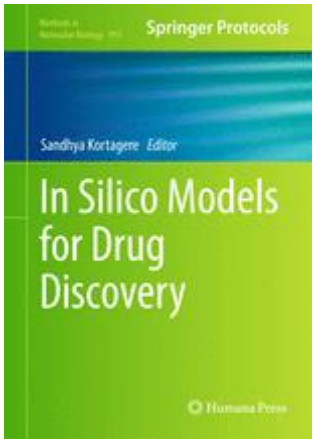


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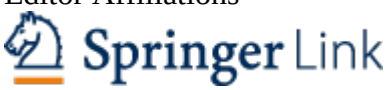

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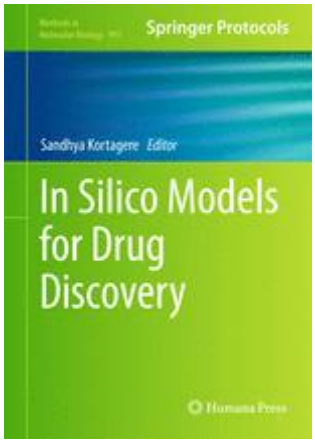


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